

Personal reflections on the Sticky Platelet Syndrome (SPS)

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Once a platelet says to his comrades: lets aggregate, let it be our way. Though the clinicians liked our clotting, we can not all the time, it is not our wish! It is our destiny. No one understands us.

G.V. Born

Sticky platelet syndrome (SPS) is a thrombophilic thrombocytopathy with familial occurrence and autosomal dominant trait, characterized by an increased in vitro platelet aggregation in response to low concentrations of adenosine diphosphate (ADP) and/or epinephrine (EPI).^{1,2} SPS was for the first time publicly described as a separate clinical syndrome by Holiday and associates at the Ninth International Joint Conference on Stroke and Cerebral Circulation in Arizona in 1983.³ The relation between platelet hyperaggregability and ischemic stroke was initially recognized by al-Mefty et al in 1979.⁴ In 1984, Mammen treated a female patient who suffered from myocardial infarction during the third trimester of her first pregnancy and in whom the extensive laboratory testing of hemostasis revealed no abnormalities except in vitro increased platelet aggregation after ADP and EPI.⁵ In the following years, Mammen and associates published their studies on a larger series of patients, defined generally accepted laboratory diagnostic criteria, and proposed two types (I and II) of the syndrome.⁵⁻⁸ In the late 2000s, Mühlfeld et al⁹ and El-Amm et al¹⁰ regarded the syndro-

me as a possible cause of thrombotic complications and impaired function of the graft in kidney transplantation. Throughout the years, several studies focused on the etiology and pathogenesis of the syndrome, but they had failed to fully reveal the genetic basis underlying the syndrome.¹¹ Physicians working in different fields of medicine were interested in the SPS research in recent years (cardiology, surgery, and ophthalmology).¹²⁻¹⁴

Since 2002 the methods for diagnosis of SPS were introduced in Martin (The National Center of Hemostasis and Thrombosis in Slovakia). Currently, our Working Group devotes to all areas of hemostasis systematically, with the main emphasis on primary hemostasis. This group composes of 11 members (Dobrotova, Holly, Chudej, Chudy, Chuda, Ivankova, Lisa, Plamenova, Stasko, Sokol and Skerenova). We appreciate international cooperation with our Czech colleagues, Danubian League against Thrombosis and Haemorrhagic Disorders (DLTH), International Society on Thrombosis and Hemostasis (ISTH) and Grupo Cooperativo Latinoamericano de Hemostasia y Trombosis (CLAHT).

Over 1500 people were examined on SPS since 2002. SPS was confirmed in 315 people. The most common clinical manifestation in our group of patients was: deep vein thrombosis, abortion, stroke, myocardial infarction, thrombophlebitis, and retinal vein occlusion. Also, we found arterial thrombosis in approximately two-thirds of all patients with SPS (with stroke and coronary syndro-

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mes). SPS Type II is the most common in our population, SPS Type III is rare. This is very interesting because both SPS Type I and III are more frequent than SPS Type II in the Mexican population.¹⁵ However, the aim of our work is not just a statistical analysis of SPS occurrence, but especially revealing its causes. It has been supposed that glycoprotein receptors on the platelet surface membrane may be involved, its abnormality leading into platelet hyperfunction. Up to now, no molecular substrate has been found to explain the platelet hyperaggregability. This being the reason why only few research groups have accepted this entity as a true thrombophilic condition. Our research had focused on GPIIIa, Gas6, and GPVI proteins. These glycoproteins were interesting because certain mutations in their genes were shown to modulate the risk of thrombosis event in humans. In our studies, we have confirmed for the first time that the SPS has probably the polygenic mode of inheritance. Each gene locus had an independent effect on a single phenotype. Therefore, hyperaggregability seems a phenotypic expression of several genes. There is an open question: are there genes of small or large effect? Further research in this area is needed. Platelets still hiding other secrets.¹¹

Despite several unresolved issues and likely infrequent prevalence in general population, sticky platelet syndrome seems to be a disorder relevant for clinical practice. With its affection of predominantly young adults, relation to fertility issues, familial occurrence, distinct laboratory diagnostics, and treatment.^{11,16}

REFERENCES

- Mammen, EF. Ten-years' experience with the "Sticky platelet syndrome". *Clin Appl Thromb Hemost* 1995;1:66-72.
- Cesarman-Maus G. Myths and reality of the sticky platelet syndrome. *Rev Hematol Mex* 2011;12:55-56.
- Holiday PL, Mammen E, Gilroy J. Sticky platelet syndrome and cerebral infarction in young adults. Paper presented at: The Ninth International Joint Conference on Stroke and Cerebral Circulation 1983; Phoenix, AZ, USA.
- al-Mefty O, Marano G, Raiaraman S, Nugent GR, Rodman N. Transient ischemic attacks due to increased platelet aggregation and adhesiveness. Ultrastructural and functional correlation. *J Neurosurg* 1979;50:449-453.
- Mammen EF. Ten years' experience with the "Sticky platelet syndrome". *Clin Appl Thromb Hemost* 1995;1:66-72.
- Rubensfire M, Blevins RD, Barnhart M, Housholder S, Selik N, Mammen EF. Platelet hyperaggregability in patients with chest pain and angiographically normal coronary arteries. *Am J Cardiol* 1986;57:657-660.
- Mammen EF, Barnhart MI, Selik NR, Gilroy J, Klepach GL. "Sticky platelet syndrome": a congenital platelet abnormality predisposing to thrombosis? *Folia Haematol Int Mag Klin Morphol Blutforsch* 1988;115:361-365.
- Mammen EF. Sticky platelet syndrome. *Semin Thromb Hemost* 1999;25: 361-365
- Mühlfeld AS, Ketteler M, Schwamborn K, et al. Sticky platelet syndrome: an underrecognized cause of graft dysfunction and thromboembolic complications in renal transplant recipients. *Am J Transplant* 2007;7:1865-1868.
- El-Amm JM, Andersen J, Gruber SA. Sticky platelet syndrome: a manageable risk factor for posttransplant thromboembolic events. *Am J Transplant* 2008;8:465.
- Kubisz P, Stasko J, Holly P. Sticky Platelet Syndrome. *Semin Thromb Hemost* 2013;39:674-683.
- Randhawa S, Van Stavern GP. Sticky platelet syndrome and arteri- or ischaemic optic neuropathy. *Clin Experiment Ophthalmol* 2007;35:779-781.
- Bojalian MO, Akingba AG, Andersen JC, et al. Sticky platelet syndrome: an unusual presentation of arterial ischemia. *Ann Vasc Surg* 2010;24:e1-e6.
- Gehoff A, Kluge JG, Gehoff P, et al. Recurrent strokes under anticoagulation therapy: Sticky platelet syndrome combined with a patent foramen ovale. *J Cardiovasc Dis Res* 2011;2:68-70.
- Ruiz-Argüelles GJ, López-Martínez B, Valdés-Tapia P, Gómez-Rangel JD, Reyes-Núñez V, Garcés-Eisele J. Primary thrombophilia in Mexico. V. A comprehensive prospective study indicates that most cases are multifactorial. *Am J Hematol* 2005;78:21-26.
- Sokol J, Biringier K, Skerenova M, Hasko M, Bartosova L, Stasko J, Danko J, Kubisz P. Platelet aggregation abnormalities in patients with fetal losses: the GP6 gene polymorphism. *Fertility and Sterility* 2012;98:1170-1174.